## (19) World Intellectual Property Organization International Bureau



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(43) International Publication Date 22 November 2001 (22.11.2001)

**PCT** 

# (10) International Publication Number WO 01/87982 A3

- (51) International Patent Classification<sup>7</sup>: C12N 15/62, C07K 19/00, C12N 15/63, 1/19, 1/21, 5/10 // C07K 16/28, 14/34
- (21) International Application Number: PCT/US01/16125
- (22) International Filing Date: 18 May 2001 (18.05.2001)
- (25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 09/573,797

18 May 2000 (18.05.2000) US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:

US Filed on 09/573,797 (CIP) 18 May 2000 (18.05.2000)

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- (75) Inventors/Applicants (for US only): NEVILLE, David,

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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

#### Published:

with international search report

(88) Date of publication of the international search report:
21 March 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

**A**3

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(54) Title: IMMUNOTOXIN FUSION PROTEINS AND MEANS FOR EXPRESSION THEREOF

(57) Abstract: The present invention described and shown in the specification and drawings provides novel recombinant DT-based immunotoxins, and, more specifically anti-T cell immunotoxin fusion proteins. Also provided are immunotoxins that can be expressed in bacterial, yeast, or mammalian cells. The invention also provides means for expression of the immunotoxin fusion protein. It is emphasized that this abstract is provided to comply with the rules requiring an abstract that will allow a searcher or other reader to quickly ascertain the subject matter of the technical disclosure. It is submitted with the understanding that it will not be used to interpret or limit the scope or meaning of the claims.

In ational Application No PCI/US 01/16125

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N15/62 C07K C07K19/00 C12N1/19 C12N1/21 C12N15/63 //C07K16/28,C07K14/34 C12N5/10 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07K A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) BIOSIS, EMBASE, CHEM ABS Data, WPI Data, PAJ, EPO-Internal, SEQUENCE SEARCH C. DOCUMENTS CONSIDERED TO BE RELEVANT Category 5 Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages X WO 98 39363 A (THE SECRETARY, DEPARTMENT 1,15-26OF HEALTH AND HUMAN SERVICES ET AL.) 29,30, 11 September 1998 (1998-09-11) 33-41. 45, 54-67. 79,80, 92-97, 116-119 examples 8-10 claims figures 11,14 Υ 31,32, 43,44, 77,78 99-103 Patent family members are listed in annex. Further documents are listed in the continuation of box C Special categories of cited documents \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the \*A\* document defining the general state of the lart which is not considered to be of particular relevance. invention earlier document but published on or after the international \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to filing date document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannol be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document reterring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled other means in the art. document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 26 November 2001 10/12/2001 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Nooij, F Fax: (+31-70) 340-3016

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In' ational Application No
PC (/US 01/16125

C.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category "	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 39425 A (THE SECRETARY, THE DEPARTMENT OF HEALTH AND HUMAN SERVICES) 11 September 1998 (1998-09-11)	31,32, 43,44, 77,78, 99-103
	the whole document	,
X	WO 96 32137 A (THE SECRETARY, THE DEPARTMENT OF HEALTH AND HUMAN SERVICES ET AL.) 17 October 1996 (1996-10-17)	1,15-26, 29,30, 33-41, 45, 54-67, 79,80, 92-97, 116-119
	examples 9-11 claims 1,22,23 	
X	J. THOMPSON ET AL.: "An anti-CD3 single-chain immunotoxin with a truncated diphtheria toxin avoids inhibition by pre-existing antibodies in human blood." THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 270, no. 47, 24 November 1995 (1995-11-24), pages 28037-28041, XP002083389 Baltimore, MD, USA the whole document	1,15-26, 33-40, 116-119
Y	the whole document	29,30, 41, 43-45, 54-67, 79,80, 92-97, 101,102
Y	S. MA ET AL.: "Expression and characterization of a divalent chimeric anti-human CD3 single-chain antibody." SCANDINAVIAN JOURNAL OF IMMUNOLOGY, vol. 43, no. 2, February 1996 (1996-02), pages 134-139, XP002083387 Oxford, GB the whole document	29,30, 41,45, 54-67, 79,80, 92-97
Y	M. KIEKE ET AL.: "Isolation of anti-T cell receptor scFv mutants by yeast surface display." PROTEIN ENGINEERING, vol. 10, no. 11, 1997, pages 1303-1310, XP002064403 Oxford, GB abstract	43,44, 101,102
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In' ational Application No
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	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	 In .
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A	D. VALLERA ET AL.: "Anti-graft-versus-host disease effect of DT390-anti-CD3sFv, a single-chain Fv fusion immunotoxin specifically targeting the CD3-epsilon moiety of the T-cell receptor." BLOOD, vol. 88, no. 6, 15 September 1996 (1996-09-15), pages 2342-2353, XP000645998 Philadelphia, PA, USA the whole document	1,15-26, 33-40, 116-119
A	S. MA ET AL.: "Genetic construction and characterization of an anti-monkey CD3 single-chain immunotoxin with a truncated diphtheria toxin." BIOCONJUGATE CHEMISTRY. vol. 8, no. 5. September 1997 (1997-09), pages 695-701. XP002183986 Washington, DC. USA abstract	1,15-26, 33-40, 116-119

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Information on patent family members

in' ational Application No
PCT/US 01/16125

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WO 9839425	Α	11-09-1998	AU AU EP WO	736501 B2 6445998 A 0968282 A2 9839425 A2	26-07-2001 22-09-1998 05-01-2000 11-09-1998
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tactacggtg atagtgactg gtacttcgat gtctggggcg caggcaccac tgtcacagtc
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atgacccaga ccacctcctc cctgtctgcc tccctgggcg acagagtcac catcagttqc
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gttaaactcc tgatctacta cacatcaaga ttacactcag gagtcccatc aaagttcagt
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ggcagtgggt ctggaacaga ttattctctc accattagca acctggagca agaggatatt
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gccacttact tttgccaaca gggtaatacg cttccgtgga cgttcgctgg aggcaccaag
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                                                                         2580
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                                                                         2640
                                                                         2700
ggaaagaacc ttgagtggat gggacttatt aatcettaca aaggtgttag tacctacaac
                                                                         2760
cagaagttca aggacaaggc cacattaact gtagacaagt catccagcac agcctacatg
                                                                         2820
gaacteetea gtetgacate tgaggactet geagtetatt actgtgeaag ateggggtae
                                                                         2880
tacggtgata gtgactggta cttcgatgtc tggggccaaq qcaccactct cacagtcttc
                                                                         2940
tcatgagaat tc
                                                                         2952
<210> 31
<211> 85
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
      synthetic construct
<400> 31
Met Arg Phe Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser
                  5
                                      10
Ala Leu Ala Ala Pro Cys Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln
                                  25
Ile Pro Ala Glu Ala Val Ile Gly Tyr Ser Asp Leu Glu Gly Asp Phe
                              40
                                                   45
Asp Val Ala Val Leu Pro Phe Ser Asn Ser Thr Asn Asn Gly Leu Leu
                         55
Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys Glu Glu Gly Val
                     70
                                          75
Ser Leu Glu Lys Arg
<210> 32
<211> 7
<212> PRT
<213> Artificial Sequence
<220>
<400> 32
Ala Ile His Arg Gly Gly Gly
<210> 33
<211> 21
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
      synthetic construct
<400> 33
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BNSDOCID: <WO\_\_\_\_0187982A2\_1\_>

gccatccacc gaggaggtgg t

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<210> 34
<211> 21
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence:/Note =
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<400> 34
Met Gly Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
Gly Ala Asp Ala Ala
            20
<210> 35
<211> 210
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence:/Note =
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                                                                       120
gtcgagtcca tcatcaactt gttccaagtc gtccacaact cctacaaccg tccggcttac
                                                                       180
                                                                       210
tccccaggtc acaagaccca accattcttg
<210> 36
<211> 21
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence:/Note =
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Met Gly Ser Ser His His His His His Ser Ser Gly Leu Val Pro
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Arg Gly Ser His Met
            20
<210> 37
<211> 6
<212> PRT
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<220>
<400> 37
Ala Ser Ala Gly Gly Ser
                 5
<210> 38
<211> 642
<212> PRT
<213> Artificial Sequence
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<400> 38 Gly Ala Asp Asp Val Val Asp Ser Ser Lys Ser Phe Val Met Glu Asn 10 Phe Ser Ser Tyr His Gly Thr Lys Pro Gly Tyr Val Asp Ser Ile Gln 25 20 Lys Gly Ile Gln Lys Pro Lys Ser Gly Thr Gln Gly Asn Tyr Asp Asp 40 Asp Trp Lys Gly Phe Tyr Ser Thr Asp Asn Lys Tyr Asp Ala Ala Gly 55 Tyr Ser Val Asp Asn Glu Asn Pro Leu Ser Gly Lys Ala Gly Gly Val Val Lys Val Thr Tyr Pro Gly Leu Thr Lys Val Leu Ala Leu Lys Val 90 8.5 Asp Asn Ala Glu Thr Ile Lys Lys Glu Leu Gly Leu Ser Leu Thr Glu 105 Pro Leu Met Glu Gln Val Gly Thr Glu Glu Phe Ile Lys Arg Phe Gly 125 120 Asp Gly Ala Ser Arg Val Val Leu Ser Leu Pro Phe Ala Glu Gly Ser 135 Ser Ser Val Glu Tyr Ile Asn Asn Trp Glu Gln Ala Lys Ala Leu Ser 150 155 Val Glu Leu Glu Ile Asn Phe Glu Thr Arg Gly Lys Arg Gly Gln Asp 170 165 Ala Met Tyr Glu Tyr Met Ala Gln Ala Cys Ala Gly Asn Arg Val Arg 185 Arg Ser Val Gly Ser Ser Leu Ser Cys Ile Asn Leu Asp Trp Asp Val 200 195 Ile Arg Asp Lys Thr Lys Thr Lys Ile Glu Ser Leu Lys Glu His Gly 215 Pro Ile Lys Asn Lys Met Ser Glu Ser Pro Asn Lys Thr Val Ser Glu 230 235 Glu Lys Ala Lys Gln Tyr Leu Glu Glu Phe His Gln Thr Ala Leu Glu 250 245 His Pro Glu Leu Ser Glu Leu Lys Thr Val Thr Gly Thr Asn Pro Val 260 265 Phe Ala Gly Ala Asn Tyr Ala Ala Trp Ala Val Asn Val Ala Gln Val 280 Ile Asp Ser Glu Thr Ala Asp Asn Leu Glu Lys Thr Thr Ala Ala Leu 300 295 Ser Ile Leu Pro Gly Ile Gly Ser Val Met Gly Ile Ala Asp Gly Ala 315 310 Val His His Asn Thr Glu Glu Ile Val Ala Gln Ser Ile Ala Leu Ser 330 325 Ser Leu Met Val Ala Gln Ala Ile Pro Leu Val Gly Glu Leu Val Asp 340 345 350 Ile Gly Phe Ala Ala Tyr Asn Phe Val Glu Ser Ile Ile Asn Leu Phe 360 365 Gln Val Val His Asn Ser Tyr Asn Arg Pro Ala Tyr Ser Pro Gly His 375 380 Lys Thr Gln Pro Phe Ala Ser Ala Gly Gly Ser Asp Ile Gln Met Thr 390 395 Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp Arg Val Thr Ile 405 410 Ser Cys Arg Ala Ser Gln Asp Ile Arg Asn Tyr Leu Asn Trp Tyr Gln 425 430 Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile Tyr Tyr Thr Ser Arg 435 440

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Leu His Ser Gly Val Pro Ser Lys Phe Ser Gly Ser Gly Ser Gly Thr
                        455
Asp Tyr. Ser Leu Thr Ile Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr
                    470
                                        475
Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Ala Gly Gly
                485
                                    490
                                                        495
Thr Lys Leu Glu Ile Lys Arg Ala Gly Gly Gly Ser Gly Gly Gly Ser
            500
                                505
                                                    510
Gly Gly Gly Ser Gly Gly Ser Glu Val Gln Leu Gln Gln Ser Gly
        515
                            520
Pro Glu Leu Val Lys Pro Gly Ala Ser Met Lys Ile Ser Cys Lys Ala
                        535
Ser Gly Tyr Ser Phe Thr Gly Tyr Thr Met Asn Trp Val Lys Gln Ser
                   550
                                        555
His Gly Lys Asn Leu Glu Trp Met Gly Leu Ile Asn Pro Tyr Lys Gly
                565
                                    570
Val Ser Thr Tyr Asn Gln Lys Phe Lys Asp Lys Ala Thr Leu Thr Val
            580
                                585
Asp Lys Ser Ser Ser Thr Ala Tyr Met Glu Leu Leu Ser Leu Thr Ser
                            600
Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser Gly Tyr Tyr Gly Asp
                        615
                                            620
Ser Asp Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val
                    630
                                        635
Ser Ser
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<210> 39

<211> 656

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:/Note =
 synthetic construct

<400> 39 Gly Ser Ser His His His His His Ser Ser Gly Leu Val Pro Arq 1 10 Gly Ser His Gly Ala Asp Asp Val Val Asp Ser Ser Lys Ser Phe Val 20 25 Met Glu Asn Phe Ser Ser Tyr His Gly Thr Lys Pro Gly Tyr Val Asp 40 Ser Ile Gln Lys Gly Ile Gln Lys Pro Lys Ser Gly Thr Gln Gly Asn 55 60 Tyr Asp Asp Asp Trp Lys Gly Phe Tyr Ser Thr Asp Asn Lys Tyr Asp 70 75 Ala Ala Gly Tyr Ser Val Asp Asn Glu Asn Pro Leu Ser Gly Lys Ala 85 90 Gly Gly Val Val Lys Val Thr Tyr Pro Gly Leu Thr Lys Val Leu Ala 105 110 Leu Lys Val Asp Asn Ala Glu Thr Ile Lys Lys Glu Leu Gly Leu Ser 120 Leu Thr Glu Pro Leu Met Glu Gln Val Gly Thr Glu Glu Phe Ile Lys 135 140 Arg Phe Gly Asp Gly Ala Ser Arg Val Val Leu Ser Leu Pro Phe Ala 150 Glu Gly Ser Ser Val Glu Tyr Ile Asn Asn Trp Glu Gln Ala Lys 170 165 Ala Leu Ser Val Glu Leu Glu Ile Asn Phe Glu Thr Arg Gly Lys Arg 185

Gly Gln Asp Ala Met Tyr Glu Tyr Met Ala Gln Ala Cys Ala Gly Asn Arg Val Arg Arg Ser Val Gly Ser Ser Leu Ser Cys Ile Asn Leu Asp Trp Asp Val Ile Arg Asp Lys Thr Lys Ile Glu Ser Leu Lys Glu His Gly Pro Ile Lys Asn Lys Met Ser Glu Ser Pro Asn Lys Thr Val Ser Glu Glu Lys Ala Lys Gln Tyr Leu Glu Glu Phe His Gln Thr Ala Leu Glu His Pro Glu Leu Ser Glu Leu Lys Thr Val Thr Gly Thr Asn Pro Val Phe Ala Gly Ala Asn Tyr Ala Ala Trp Ala Val Asn Val Ala Gln Val Ile Asp Ser Glu Thr Ala Asp Asn Leu Glu Lys Thr Thr Ala Ala Leu Ser Ile Leu Pro Gly Ile Gly Ser Val Met Gly Ile Ala Asp Gly Ala Val His His Asn Thr Glu Glu Ile Val Ala Gln Ser Ile Ala Leu Ser Ser Leu Met Val Ala Gln Ala Ile Pro Leu Val Gly Glu Leu Val Asp Ile Gly Phe Ala Ala Tyr Asn Phe Val Glu Ser Ile Ile Asn Leu Phe Gln Val Val His Asn Ser Tyr Asn Arg Pro Ala Tyr Ser Pro Gly His Lys Thr Gln Pro Phe Leu Pro Trp Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Arg Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Lys Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Ala Gly Gly Thr Lys Leu Glu Ile Lys Arg Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala Ser Met Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Met Gly Leu Ile Asn Pro Tyr Lys Gly Val Ser Thr Tyr Asn Gln Lys Phe Lys Asp Lys Ala Thr Phe Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr Met Glu Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser Gly Tyr Tyr Gly Asp Ser Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Leu Thr Val Phe Ser 

<210> 40 <211> 1943 <212> DNA

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<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
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<400> 40
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cgtaccacgg gactaaacct ggttatgtag attccattca aaaaggtata caaaagccaa
                                                                         120
aatctggtac acaaggaaat tatgacgatg attggaaagg gttttatagt accgacaata
                                                                         180
aatacgacgc tgcgggatac tctgtagata atgaaaaccc gctctctgga aaagctggag
                                                                         240
gcqtggtcaa agtgacgtat ccaqqactqa cqaaqqttct cqcactaaaa qtqqataatq
                                                                         300
ccgaaactat taagaaagag ttaggtttaa gtctcactga accgttgatg gagcaagtcg
                                                                         360
                                                                         420
gaacggaaga gtttatcaaa aggttcggtg atggtgcttc gcgtgtagtg ctcagccttc
ccttcgctga ggggagttct agcgttgaat atattaataa ctgggaacag gcgaaagcgt
                                                                         480
taagcgtaga acttgagatt aattttgaaa cccgtggaaa acgtggccaa gatgcgatgt
                                                                         540
atgagtatat ggctcaagcc tgtgcaggaa atcgtgtcag gcgatcagta ggtagctcat
                                                                         600
tgtcatgcat aaatcttgat tgggatgtca taagggataa aactaagaca aagatagagt
                                                                         660
                                                                         720
ctttgaaaga gcatggccct atcaaaaata aaatgagcga aagtcccaat aaaacagtat
ctgaggaaaa agctaaacaa tacctagaag aatttcatca aacggcatta gagcatcctg
                                                                         780
aattgtcaga acttaaaacc gttactggga ccaatcctgt attcgctggg gctaactatg
                                                                         840
cggcgtgggc agtaaacgtt gcgcaagtta tcgatagcga aacagctgat aatttggaaa
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agacaactgc tgctctttcg atacttcctg gtatcggtag cgtaatgggc attgcagacg
                                                                         960
gigccgttca ccacaataca gaagagatag iggcacaatc aatagctita tcgictitaa
                                                                        1020
tggttgctca agctattcca ttggtaggag agctagttga tattggtttc gctgcatata
                                                                        1080
attttgtaga gagtattatc aatttatttc aagtagttca taattcgtat aatcgtcccg
                                                                        1140
cgtattctcc ggggcataaa acgcaaccat ttgcttccgc cggtggatcc gacatccaga
                                                                        1200
tgacccagac cacctcctcc ctgtctgcct ctctgggaga cagagtcacc atcagttgca
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gggcaagtca ggacattaga aattatttaa actggtatca acagaaacca gatggaactg
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ttaaactcct gatctactac acatcaagat tacactcagg agtcccatca aagttcagtg
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gcagtgggtc tggaacagat tattctctca ccattagcaa cctggagcaa gaggatattg
                                                                        1440
ccacttactt ttgccaacag ggtaatacgc ttccgtggac gttcgctgga ggcaccaagc
                                                                        1500
tggaaatcaa acgggctgga ggcggtagtg gcggtggatc aggtggaggc agcggtggcg
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gatctgaggt gcagctccag cagtctggac ctgagctggt gaagcctgga gcttcaatga
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cctacaacca gaagttcaag gacaaggcca cattaactgt agacaagtca tccagcacag
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cctacatgga actcctcagt ctgacatctg aggactctgc agtctattac tgtgcaagat
                                                                        1860
eggggtacta eggtgatagt gactggtact tegatgtetg gggegeaggg accaeggtea
                                                                        1920
                                                                        1943
ccgtctcctc atgatagaga tct
<210> 41
<211> 1940
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
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accacgggac taaacctggt tatgtagatt ccattcaaaa aggtatacaa aagccaaaat
                                                                         120
ctggtacaca aggaaattat gacgatgatt ggaaagggtt ttatagtacc gacaataaat
                                                                         180
acgacgctgc gggatactct gtagataatg aaaacccgct ctctggaaaa gctggaggcg
                                                                         240
tggtcaaagt gacgtatcca ggactgacga aggttctcgc actaaaagtg gataatgccg
                                                                         300
aaactattaa gaaagagtta ggtttaagtc tcactgaacc gttgatggag caagtcggaa
                                                                         360
cggaagagtt tatcaaaagg ttcggtgatg gtgcttcgcg tgtagtgctc agccttccct tcgctgaggg gagttctagc gttgaatata ttaataactg ggaacaggcg aaagcgttaa
                                                                         420
                                                                         480
gcgtagaact tgagattaat tttgaaaccc gtggaaaacg tggccaagat gcgatgtatg
                                                                         540
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catgcataaa tottgattqq qatgtcataa gggataaaac taagacaaag atagagtott
                                                                         660
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780 840

900

960

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                                                                      1140
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                                                                      1200
cccagaccac ctcctcctg tctgcctctc tgggagacag agtcaccatc agttgcaggg
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caagtcagga cattagaaat tatttaaact ggtatcaaca gaaaccagat ggaactgtta
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                                                                      1740
acaaccagaa gttcaaggac aaggccacat taactgtaga caagtcatcc agcacagcct
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acatggaact cctcagictg acatctgagg actctgcagt ctattactgt gcaagaicgg
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                                                                      1920
tctcctcatg atagagatct
                                                                      1940
<210> 42
<211> 24
<212> DNA
<213> Artificial Sequence
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Pro Gly Pro Thr Asn Ser His Tyr
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<211> 15
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
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<400> 43
<210> 44
<211> 63
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
      synthetic construct
<400> 44
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                                                                         63
<210> 45
<211> 57
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
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<210> 46
<211> 56
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
      synthetic construct
<400> 46
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                                                                         56
<210> 47
<211> 8
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
      synthetic construct
<400> 47
Glu Ala Glu Ala Tyr Val Glu Phe
<210> 48
<211> 6
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
      synthetic construct
<400> 48
Glu Ala Tyr Val Glu Phe
 1
                 5
<210> 49
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
      synthetic construct
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<210> <211> <212> <213>	30	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
<400> tataco	50 catgg gcgctgatga tgttgttgat	30
<210> <211> <212> <213>	23	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
<400> actgc	51 ccacg ccgcatagtt agc	23
<210> <211> <212> <213>	38	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
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<210> <211> <212> <213>	33	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
<400> cgctat	53 cgat aacttgcgca acgtttactg ccc	33
<210> <211> <212> <213>	44	
<400>		
acaatt	gtot titocaaati atcagotgit togotatoga taac	44

<210> <211> <212> <213>	46	
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<400> gctaco	55 cgata ccaggaagta tcgaaagagc agcagttgtc ttttcc	46
<210> <211> <212> <213>	57	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
<400> gaacgg	56 gcacc gtctgcaatg cccattacgc taccgatacc aggaagtatc gaaagag	57
<210> <211> <212> <213>	42	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
<400> actato	57 ctctt ctgtattgtg gtgaacggca ccgtctgcaa tg	42
<210> <211> <212> <213>	48	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
<400> caacca	58 attaa agacgataaa gctattgatt gtgccactat ctcttctg	48
<210><211><211><212><213>	80	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
	59 aaatt atatgcagcg aaaccaatat caactagctc tectaccaat ggaatagctt accat taaagacgat	60 80
<210>	60	

<211> (<212> )<212> )		
	Description of Artificial Sequence:/Note = synthetic construct	
<400> cgatta: gcagcg	tacg aattatgaac tacttgaaat aaattgataa tactctctac aaaattatat	60 66
<210> (<211> )<211> )<212> )<213> )	83	
<220> <223>	Description of Artificial Sequence:/Note =	
	synthetic construct	
	61 tcgg atccaccggc ggaagcaaat ggttgcgttt tatgccccgg agaatacgcg ttat acgaattatg aac	60 83
<210> <211> <212> <213>	83	
	Description of Artificial Sequence:/Note = synthetic construct	
	62 tcgg atccaccggc ggaagcaaat ggttgcgttt tatgccccgg agaatacgcg ttat acgaattatg aac	60 83
<210><211><211><212><213>	41 .	
	Description of Artificial Sequence:/Note = synthetic construct	
<400> aagtag	63 ttca taattogtat aatogtooog ogtattotoo g	41
<210> <211> <212> <213>	32	
	Description of Artificial Sequence:/Note = synthetic construct	
<400> gcggat	64 ccga catccagatg acccagacca cc	32

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<210> 65
<211> 32
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
      synthetic construct
<400> 65
cctctagaag cccgtttgat ttccagcttg gt
                                                                         32
<210> 66
<211> 29
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
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<400> 66
ccgtcgacga ggtgcagctc cagcagtct
                                                                         29
<210> 67
<211> 35
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
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<400> 67
ccaagettte atgaggagae ggtgaeegtg gteee
                                                                         35
<210> 68
<211> 657
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence:/Note =
      synthetic construct
<400> 68
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                                     10
Arg Gly Ser His Gly Ala Asp Asp Val Val Asp Ser Ser Lys Ser Phe
            20
                                 25
Val Met Glu Asn Phe Ser Ser Tyr His Gly Thr Lys Pro Gly Tyr Val
        35
                             40
Asp Ser Ile Gln Lys Gly Ile Gln Lys Pro Lys Ser Gly Thr Gln Gly
                        55
Asn Tyr Asp Asp Asp Trp Lys Gly Phe Tyr Ser Thr Asp Asn Lys Tyr
                    70
                                         75
Asp Ala Ala Gly Tyr Ser Val Asp Asn Glu Asn Pro Leu Ser Gly Lys
                85
                                     90
Ala Gly Gly Val Val Lys Val Thr Tyr Pro Gly Leu Thr Lys Val Leu
                                 105
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110

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PCT/US01/16125

Ala Leu Lys Val Asp Asn Ala Glu Thr Ile Lys Lys Glu Leu Gly Leu Ser Leu Thr Glu Pro Leu Met Glu Gln Val Gly Thr Glu Glu Phe Ile Lys Arg Phe Gly Asp Gly Ala Ser Arg Val Val Leu Ser Leu Pro Phe Ala Glu Gly Ser Ser Ser Val Glu Tyr Ile Asn Asn Trp Glu Gln Ala Lys Ala Leu Ser Val Glu Leu Glu Ile Asn Phe Glu Thr Arg Gly Lys Arg Gly Gln Asp Ala Met Tyr Glu Tyr Met Ala Gln Ala Cys Ala Gly Asn Arg Val Arg Arg Ser Val Gly Ser Ser Leu Ser Cys Ile Asn Leu Asp Trp Asp Val Ile Arg Asp Lys Thr Lys Thr Lys Ile Glu Ser Leu Lys Glu His Gly Pro Ile Lys Asn Lys Met Ser Glu Ser Pro Asn Lys Thr Val Ser Glu Glu Lys Ala Lys Gln Tyr Leu Glu Glu Phe His Gln Thr Ala Leu Glu His Pro Glu Leu Ser Glu Leu Lys Thr Val Thr Gly Thr Asn Pro Val Phe Ala Gly Ala Asn Tyr Ala Ala Trp Ala Val Asn Val Ala Gln Val Ile Asp Ser Glu Thr Ala Asp Asn Leu Glu Lys Thr Thr Ala Ala Leu Ser Ile Leu Pro Gly Ile Gly Ser Val Met Gly Ile Ala Asp Gly Ala Val His His Asn Thr Glu Glu Ile Val Ala Gln Ser Ile Ala Leu Ser Ser Leu Met Val Ala Gln Ala Ile Pro Leu Val Gly Glu Leu Val Asp Ile Gly Phe Ala Ala Tyr Asn Phe Val Glu Ser Ile Ile Asn Leu Phe Gln Val Val His Asn Ser Tyr Asn Arg Pro Ala Tyr Ser Pro Gly His Lys Thr Gln Pro Phe Leu Pro Trp Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Arg Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Lys Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Glu Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Ala Gly Gly Thr Lys Leu Glu Ile Lys Arg Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala Ser Met Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Met Gly Leu Ile Asn Pro Tyr Lys Gly Val Ser Thr Tyr Asn Gln Lys Phe Lys Asp Lys Ala Thr Phe Thr Val Asp 

```
Lys Ser Ser Ser Thr Ala Tyr Met Glu Leu Leu Ser Leu Thr Ser Glu 610 615 620

Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser Gly Tyr Tyr Gly Asp Ser 625 630 630 640

Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Leu Thr Val Phe 645 655

Ser
```

<210> 69 <211> 643 <212> PRT <213> Artificial Sequence

<400> 69 Met Gly Ala Asp Asp Val Val Asp Ser Ser Lys Ser Phe Val Met Glu Asn Phe Ser Ser Tyr His Gly Thr Lys Pro Gly Tyr Val Asp Ser Ile 20 25 30 Gln Lys Gly Ile Gln Lys Pro Lys Ser Gly Thr Gln Gly Asn Tyr Asp 40 Asp Asp Trp Lys Gly Phe Tyr Ser Thr Asp Asn Lys Tyr Asp Ala Ala 55 60 Gly Tyr Ser Val Asp Asn Glu Asn Pro Leu Ser Gly Lys Ala Gly Gly 75 Val Val Lys Val Thr Tyr Pro Gly Leu Thr Lys Val Leu Ala Leu Lys 85 90 Val Asp Asn Ala Glu Thr Ile Lys Lys Glu Leu Gly Leu Ser Leu Thr 100 105 Glu Pro Leu Met Glu Gln Val Gly Thr Glu Glu Phe Ile Lys Arg Phe 115 120 Gly Asp Gly Ala Ser Arg Val Val Leu Ser Leu Pro Phe Ala Glu Gly 135 140 Ser Ser Ser Val Glu Tyr Ile Asn Asn Trp Glu Gln Ala Lys Ala Leu 150 155 Ser Val Glu Leu Glu Ile Asn Phe Glu Thr Arg Gly Lys Arg Gly Gln 165 170 175 Asp Ala Met Tyr Glu Tyr Met Ala Gln Ala Cys Ala Gly Asn Arg Val 180 185 Arg Arg Ser Val Gly Ser Ser Leu Ser Cys Ile Asn Leu Asp Trp Asp 195 200 205 Val Ile Arg Asp Lys Thr Lys Thr Lys Ile Glu Ser Leu Lys Glu His 215 Gly Pro Ile Lys Asn Lys Met Ser Glu Ser Pro Asn Lys Thr Val Ser 230 235 Glu Glu Lys Ala Lys Gln Tyr Leu Glu Glu Phe His Gln Thr Ala Leu 245 250 Glu His Pro Glu Leu Ser Glu Leu Lys Thr Val Thr Gly Thr Asn Pro 260 265 270 Val Phe Ala Gly Ala Asn Tyr Ala Ala Trp Ala Val Asn Val Ala Gln 280 285 Val Ile Asp Ser Glu Thr Ala Asp Asn Leu Glu Lys Thr Thr Ala Ala 295 300

```
Leu Ser Ile Leu Pro Gly Ile Gly Ser Val Met Gly Ile Ala Asp Gly
                    310
                                        315
Ala Val His His Asn Thr Glu Glu Ile Val Ala Gln Ser Ile Ala Leu
                325
                                    330
Ser Ser Leu Met Val Ala Gln Ala Ile Pro Leu Val Gly Glu Leu Val
                                345
Asp Ile Gly Phe Ala Ala Tyr Asn Phe Val Glu Ser Ile Ile Asn Leu
        355
                           360
                                                365
Phe Gln Val Val His Asn Ser Tyr Asn Arg Pro Ala Tyr Ser Pro Gly
                        375
                                            380
His Lys Thr Gln Pro Phe Ala Ser Ala Gly Gly Ser Asp Ile Gln Met
                    390
                                        395
Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp Arg Val Thr
                                   410
               405
Ile Ser Cys Arg Ala Ser Gln Asp Ile Arg Asn Tyr Leu Asn Trp Tyr
                                425
Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile Tyr Tyr Thr Ser
                                                445
                           440
       435
Arg Leu His Ser Gly Val Pro Ser Lys Phe Ser Gly Ser Gly Ser Gly
                        455
                                            460
Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Glu Glu Asp Ile Ala
                    470
                                        475
Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Ala Gly
                485
                                    490
Gly Thr Lys Leu Glu Ile Lys Arg Ala Gly Gly Gly Ser Gly Gly Gly
                                505
                                                    510
Ser Gly Gly Gly Ser Gly Gly Ser Glu Val Gln Leu Gln Gln Ser
                            520
        515
                                                525
Gly Pro Glu Leu Val Lys Pro Gly Ala Ser Met Lys Ile Ser Cys Lys
                        535
                                            540
Ala Ser Gly Tyr Ser Phe Thr Gly Tyr Thr Met Asn Trp Val Lys Gln
                                        555
                    550
Ser His Gly Lys Asn Leu Glu Trp Met Gly Leu Ile Asn Pro Tyr Lys
                565
                                    570
                                                        575
Gly Val Ser Thr Tyr Asn Gln Lys Phe Lys Asp Lys Ala Thr Leu Thr
                                585
            580
Val Asp Lys Ser Ser Ser Thr Ala Tyr Met Glu Leu Leu Ser Leu Thr
        595
                            600
Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser Gly Tyr Tyr Gly
                                            620
                        615
Asp Ser Asp Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr
                    630
Val Ser Ser
```

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<210> 70
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<220>

<223> Description of Artificial Sequence:/Note =
 synthetic construct

<400> 70

Met Ser Glu Ser Pro Asn Lys Thr Val Ser Glu Glu
1 10

<sup>&</sup>lt;211> 12

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Artificial Sequence

<210><211><211><212><213>	36	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
<400> atgago	71 gaaa gtcccaataa aacagtatct gaggaa	36
<210> <211> <212> <213>	32	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
<400> gagcga	72 aaagt ccccagaaga cagtatctga gg	32
<210> <211> <212> <213>	12	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
<400> gaagad	73 egaag ac	12
<210> <211> <212>	36	
<213>	Artificial Sequence	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
<400> gtcttd	74 egtet tegtettegt ettegtette gtette	36
<210> <211> <212> <213>	12	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	

<400> Met So 1	75 er Glu Ser Pro Asn Lys Thr Val Ser Glu Glu 5 10	
<210> <211> <212> <213>	36	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
<400> atgage	76 cgaaa gtcccaataa aacagtatct gaggaa	36
<210> <211> <212> <213>	32	
<220> <223>	Description of Artificial Sequence:/Note = synthetic construct	
<400> gagcga	77 aaagt ccggccaaaa cagtatctga gg	32
<210> <211> <212> <213>	6	
<220> <223>	Description of Artificial Sequence:/Note =	
	synthetic construct	
<400> cggcca		6
<210> <211> <212> <213>	6	
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<400> tggccg		6
<210> <211> <212> <213>	14	

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<210> 81
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<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
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<400> 81
                                                                         42
atgagcgaaa gtcccaataa aacagtatct gaggaaaaac ct
<210> 82
<211> 39
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
      synthetic construct
                                                                         39
gagcgaaagt cccaataaag cggtctctga ggaaaaacc
<210> 83
<211> 6
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
      synthetic construct
<400> 83
                                                                           6
ggtctc
<210> 84
<211> 30
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
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<400> 84
gagaccgaga ccgagaccga gaccgagacc
                                                                         30
<210> 85
<211> 12
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<212> PRT <213> Artificia	l Sequence			
	on of Artificial construct	Sequence:/Note	=	
<400> 85 Ser Phe Val Met 1	Glu Asn Phe Ser 5	Ser Tyr His Gly 10	,	
<210> 86 <211> 36 <212> DNA <213> Artificia	l Sequence			
	on of Artificial construct	Sequence:/Note	=	
<400> 86 tcttttgtga tgga:	aaactt ttcttcgtac	cacggg		36
<210> 87 <211> 33 <212> DNA <213> Artificia	l Sequence			
	on of Artificial construct	Sequence:/Note	=	
<400> 87 cttttgtgat ggaa	getttt tettegtace	acg		33
<210> 88 <211> 6 <212> DNA <213> Artificia	1 Sequence			
	on of Artificial construct	Sequence:/Note	=	
<400> 88 aagctt				. 6
<210> 89 <211> 6 <212> DNA <213> Artificia.	l Sequence			
	on of Artificial construct	Sequence:/Note	=	
<400> 89 aagctt				. 6

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<210> 90
<211> 14
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
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Phe Val Met Glu Asn Phe Ser Ser Tyr His Gly Thr Lys Pro
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<210> 91
<211> 42
<212> DNA
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<223> Description of Artificial Sequence:/Note =
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tttgtgatgg aaaacttttc ttcgtaccac gggactaaac ct
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<210> 92
<211> 38
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
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<400> 92
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                                                                         38
<210> 93
<211> 6
<212> DNA
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<223> Description of Artificial Sequence:/Note =
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<400> 93
                                                                          6
gctagc
<210> 94
<211> 6
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/Note =
      synthetic construct
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<400> 94 gctagc	6
<210> 95 <211> 180 <212> DNA <213> Artificial Sequence	
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<210> 96 <211> 180 <212> DNA <213> Artificial Sequence	
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<210> 97 <211> 120 <212> DNA <213> Artificial Sequence	
<220> <223> Description of Artificial Sequence:/Note = synthetic construct	
<400> 97 aaagagcatg gccctatcaa aaataaaatg agcgaaagtc ccaataaaac agtatctgag gaaaaagcta aacaatacct agaagaattt catcaaacgg cattagagca tcctgaattg	60 120
<210> 98 <211> 120 <212> DNA <213> Artificial Sequence	
<220> <223> Description of Artificial Sequence:/Note = synthetic construct	
<400> 98 aaagagcatg gcccaatcaa gaacaagatg tccgaatccc ccgctaagac cgtctccgag	60 120

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<210> 99
<211> 210
<212> DNA
<213> Artificial Sequence
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<223> Description of Artificial Sequence:/Note =
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gctcaagcta ttccattggt aggagagcta gttgatattg gtttcgctgc atataatttt
                                                                       120
gtagagagta ttatcaattt atttcaagta gttcataatt cgtataatcg tcccgcgtat
                                                                       180
                                                                       210
tctccggggc ataaaacgca accatttctt
<210> 100
<211> 56
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/note =
      synthetic construct
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<210> 101
<211> 21
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/note =
      synthetic construct
<400> 101
                                                                        21
gccgatgcta tccacagaag a
<210> 102
<211> 2691
<212> DNA
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<223> Description of Artificial Sequence:/note =
      synthetic construct
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                                                                        60
taccacggga ccaagccagg ttacgtcgac tccatccaga agggtatcca gaagccaaag
                                                                       120
teeggeacee aaggtaacta egacgaegae tggaaggggt tetacteeae egacaacaag
                                                                       180
tacgacgctg cgggatactc tgtagataat gaaaacccgc tctctggaaa agctggaggc
                                                                       240
gtggtcaagg tcacctaccc aggtctgact aaggtcttgg ctttgaaggt cgacaacgct
                                                                       300
gagaccatca agaaggagtt gggtttgtcc ttgactgagc cattgatgga gcaagtcggt
                                                                       360
accgaagagt tcatcaagag attcggtgac ggtgcttcca gagtcgtctt gtccttgcca
                                                                       420
ttcgctgagg gttcttctag cgttgaatat attaataact gggaacaggc taaggctttg
                                                                       480
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540
tctgttgaat tggagattaa cttcgaaacc agaggtaaga gaggtcaaga tgcgatgtat
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tectgtatea acctagactg ggacgteate agagacaaga etaagaceaa gategagtet
                                                                          660
ttgaaagage atggeecaat caagaacaag atgteegaat ceeeegetaa gaeegtetee
                                                                          720
gaggaaaagg ccaagcaata cctagaagag ttccaccaaa ccgccttgga gcatcctgaa
                                                                          780
                                                                          840
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qcqtqqqcaq taaacqttqc qcaaqttatc gatagcgaaa cagctgataa tttggaaaag
                                                                          960
acaactgctg ctctttcgat acttcctggt atcggtagcg taatgggcat tgcagacggt
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                                                                         1020
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                                                                         1200
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                                                                         1260
gacatcagaa actacttgaa ctggtatcag cagaagccag acggtactgt caagttgttg
                                                                         1320
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                                                                         1380
ggtactgact actccttgac catctccaac ttggagcaag aggatattgc cacttacttt
                                                                         1440
                                                                         1500
toccaacago qtaatacget teegtggacg ttegetggag geaccaagtt ggagatcaag
ggtggaggag gttctggagg tggtggatct ggaggtggag gttctgaggt tcaattgcaa
                                                                         1560
caatctggac ctgagctggt gaagcctgga gcttcaatga agatatcctg caaggcttct
                                                                         1620
ggttactcat tcactggcta caccatgaac tgggtgaagc agagtcatgg aaagaacctt
                                                                         1680
gagtggatgg gtttgattaa cccttacaag ggtgtctcga cctacaacca gaagttcaag gacaaggcta ctttcactgt agacaagtca tccagcacag cctacatgga actcctcagt
                                                                         1740
                                                                         1800
ctgacatctg aggactctgc agtctattac tgtgcaagat cggggtacta cggtgatagt
                                                                         1860
gactggtact tcgatgtctg gggtgctggt actactgtca ctgtctcctc tggaggtgga
                                                                         1920
ggatciggag gaggiggitc iggiggigga ggitcigaca iccagaigac ccagaccacc
                                                                         1980
                                                                         2040
tectecetgt etgeeteeet gggegaeaga gteaceatea gttgeaggge aagteaggae
                                                                         2100
atcagaaact acttgaactg gtatcagcag aagccagacg gtactgtcaa gttgttgatc
tactacactt ccagattgca ctctggtgtc ccatctaagt tctctggatc tggttctggt
                                                                         2160
actgactact ccttgaccat ctccaacttg gagcaagagg atattgccac ttacttttgc
                                                                         2220
caacagggta atacgcttcc gtggacgttc gctggaggca ccaagttgga gatcaagggt
                                                                         2280
ggaggaggtt ctggaggtgg tggatctgga ggtggaggtt ctgaggttca attgcaacaa
                                                                         2340
tetggaeetg agetggtgaa geetggaget teaatgaaga tateetgeaa ggettetggt
                                                                         2400
tactcattca ctggctacac catgaactgg gtgaagcaga gtcatggaaa gaaccttgag
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tggatgggtt tgattaaccc ttacaagggt gtctcgacct acaaccagaa gttcaaggac
                                                                         2520
                                                                         2580
aaggetaett teaetgtaga caagteatee ageacageet acatggaaet ceteagtetg
acatctgagg actctgcagt ctattactgt gcaagatcgg ggtactacgg tgatagtgac
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                                                                         2691
<210> 103
<211> 20
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/note =
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<400> 103
Met Ser Val Pro Thr Gln Val Leu Gly Leu Leu Leu Trp Leu Thr
                                      10
Asp Ala Arg Cys
<210> 104
<211> 16
<212> PRT
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<213> Artificial Sequence

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<220>
<223> Description of Artificial Sequence:/note =
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Gly Gly Gly Ser Gly Gly Ser Gly Gly Gly Ser Gly Gly Ser
                                    10
<210> 105
<211> 15
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:/note =
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<400> 105
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
                  5
                                     10
                                                        15
<210> 106
<211> 5
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence:/note =
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Met Leu Ala Asp Asp
<210> 107
<211> 4
<212> PRT
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<400> 107
Met Leu Asp Asp
<210> 108
<211> 4
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence:/note =
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<400> 108
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Ser Ala Asp Asp

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1
<210> 109
<211> 6
<212> PRT
<213> Artificial Sequence
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<210> 110
<211> 4
<212> PRT
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 1
<210> 111
<211> 5
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Met Gly Ala Asp Asp
 1
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Gln Lys Gly Ile Gln Lys Pro Lys Ser Gly Thr Gln Gly Asn Tyr Asp
        35
                            40
Asp Asp Trp Lys Gly Phe Tyr Ser Thr Asp Asn Lys Tyr Asp Ala Ala
                                             60
                         55
Gly Tyr Ser Val Asp Asn Glu Asn Pro Leu Ser Gly Lys Ala Gly Gly
                                         75
                    70
Val Val Lys Val Thr Tyr Pro Gly Leu Thr Lys Val Leu Ala Leu Lys
                85
                                     90
Val Asp Asn Ala Glu Thr Ile Lys Lys Glu Leu Gly Leu Ser Leu Thr
                                105
                                                     110
            100
Glu Pro Leu Met Glu Gln Val Gly Thr Glu Glu Phe Ile Lys Arg Phe
                             120
Gly Asp Gly Ala Ser Arg Val Val Leu Ser Leu Pro Phe Ala Glu Gly
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                         135
                                             140
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Ser Ser Ser Val Glu Tyr Ile Asn Asn Trp Glu Gln Ala Lys Ala Leu Ser Val Glu Leu Glu Ile Asn Phe Glu Thr Arg Gly Lys Arg Gly Gln Asp Ala Met Tyr Glu Tyr Met Ala Gln Ala Cys Ala Gly Asn Arg Val Arg Arg Ser Val Gly Ser Ser Leu Ser Cys Ile Asn Leu Asp Trp Asp Val Ile Arg Asp Lys Thr Lys Thr Lys Ile Glu Ser Leu Lys Glu His Gly Pro Ile Lys Asn Lys Met Ser Glu Ser Pro Ala Lys Thr Val Ser Glu Glu Lys Ala Lys Gln Tyr Leu Glu Glu Phe His Gln Thr Ala Leu Glu His Pro Glu Leu Ser Glu Leu Lys Thr Val Thr Gly Thr Asn Pro Val Phe Ala Gly Ala Asn Tyr Ala Ala Trp Ala Val Asn Val Ala Gln Val Ile Asp Ser Glu Thr Ala Asp Asn Leu Glu Lys Thr Thr Ala Ala Leu Ser Ile Leu Pro Gly Ile Gly Ser Val Met Gly Ile Ala Asp Gly Ala Val His His Asn Thr Glu Glu Ile Val Ala Gln Ser Ile Ala Leu Ser Ser Leu Met Val Ala Gln Ala Ile Pro Leu Val Gly Glu Leu Val Asp Ile Gly Phe Ala Ala Tyr Asn Phe Val Glu Ser Ile Ile Asn Leu Phe Gln Val Val His Asn Ser Tyr Asn Arg Pro Ala Tyr Ser Pro Gly His Lys Thr Gln Pro Phe Leu Pro Trp Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Arg Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Lys Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp Thr Phe Ala Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser. Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala Ser Met Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Met Gly Leu Ile Asn Pro Tyr Lys Gly Val Ser Thr Tyr Asn Gln Lys Phe Lys Asp Lys Ala Thr Phe Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr Met Glu Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val 

Gly Ser Asp Asp

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Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Gly Gly
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